

Inventors: Border and Ruoslahti
Serial No.: 08/349,479
Filed: December 2, 1994
Page 2

Sub
LI
II
whereby the binding of the anti-TGF- β antibody to
the TGF- β suppresses the deleterious accumulation of the TGF-
 β -induced extracellular matrix in the tissue.

REMARKS

By the present communication, claim 21 has been amended to define Applicants' invention with greater particularity. No new matter is introduced by the subject amendments as all amended claim language is fully supported by the specification.

It is respectfully submitted that the provisional rejections of claims 21-23 and 25 under the doctrine of obviousness-type double patenting as allegedly unpatentable over copending application Serial Nos. 08/407,942; 08/459,865; and 08/457,707, has been rendered moot by the Terminal Disclaimer submitted herewith as Attachment A.

The rejection of claims 21-23 and 25 under 35 U.S.C. §112, second paragraph, is respectfully traversed. It is respectfully submitted that the Examiner's concern with respect to the phrase "characterized by" has been rendered moot by the amendments submitted herewith substantially as suggested. The Examiner's suggestion of acceptable alternative claim language is acknowledged with appreciation. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Inventors: Border and Ruoslahti
Serial No.: 08/349,479
Filed: December 2, 1994
Page 3

The rejections of claims 21 under 35 U.S.C. §103 as allegedly unpatentable over Conner et al., J. Clin. Invest., 83:1661-1666 (May/1989), and of claims 22 and 23 over Conner et al., supra, in view of MacKay et al., J. Clin. Invest., 83:1160-1167 (April/1989), is respectfully traversed.

It is respectfully submitted that the Rule 131 Declaration submitted herewith as Attachment B establishes that Applicants conceived of the claimed methods prior to the publication dates of both Conner and Mackay references, and that Applicants were diligent in reducing the claimed invention to practice. The inventors explicit averments under oath, and Exhibits A-D establish conception of the claimed methods. For example, Exhibit C of the Declaration is a copy of a letter from Dr. Ruoslahti to Dr. Border prior to December 22, 1988, in which Dr. Ruoslahti discusses results observed in the experiments described in Exhibit B, pages 2 and 3 of the Declaration, related to "the inhibition of TGF β effects by PDGF" and "the inhibition of TGF β effects by RGD." The inventors state under oath that:

In addition to PDGF and RGD peptides as inhibitors of TGF β , we had also contemplated, prior to December 22, 1988, anti-TGF β antibody as another agent that could bind to TGF β in a tissue and inhibit TGF β effects to treat pathologies, as demonstrated by the Experiment related to Exhibit B, page 1.

See Accompanying Rule 131 Declaration at paragraph 9.

Inventors: Border and Ruoslahti
Serial No.: 08/349,479
Filed: December 2, 1994
Page 4

In addition, Exhibit D of the Declaration, at Section A.2.f. of page 13 of the Grant Application of Dr. Border titled "Growth Factors and Extracellular Matrix in Glomerular Disease," in the section related to a Research Plan-Specific Aim, in vivo, where it is explicitly stated that the inventors conceived:

To develop regimens for therapeutic intervention in the disease model by antibodies and other agents capable of neutralizing the TGF β effect.

In addition, Exhibit D of the Declaration, at paragraph "e." of page 27 of Dr. Border's Grant Application, in the section related to Experimental Design and Methods, explicitly states that:

We have proposed several experiments that may provide agents that could block or ameliorate the action of TGF β in the animal model of mesangial injury...It is **conceivable** that one or more of these agents could be administered to the animal and/or infused directly into the kidney as therapeutic agents to prevent the expansion of mesangial matrix...We expect that one or more of the agents to be tested will block the action of TGF β . This information would be immediately applicable to the design of a study to treat humans with glomerulonephritis.

Thus, it is respectfully submitted that Applicants conceived of contacting tissue with an anti-TGF- β antibody that binds to TGF- β , in vivo, for treating a pathology prior to the Conner and Mackay publication dates.

Inventors: Border and Ruoslahti
Serial No.: 08/349,479
Filed: December 2, 1994
Page 5

Moreover, regarding the inventors explicit statement under oath that they conceived the claimed methods prior to December 22, 1988, Dr. Border was an attending physician of glomerulonephritis patients prior to his work on the instant invention, during his work on the present invention, and still treats such patients today. The whole purpose of Dr. Border's collaboration with Dr. Ruoslahti was to identify new methods of treating patients with pathology.

It is respectfully submitted that Exhibits A, D and E establish diligence in reducing the claimed invention to practice from the time of bleeding the anti-TGF β producing animals December 13-21, 1988 (Exhibit A), through the Grant Application period, through the drafting of the manuscript on August 28, 1989. The manuscript (Exhibit E) summarizes the results of experiments conducted, as set forth in Example VII of the specification, subsequent to the submission of the Grant Application (Exhibit D). Thus, the Conner and MacKay publications have been antedated and cannot be used as prior art. Accordingly, these rejections have been rendered moot.

The rejections of claims 21-23 and 25 under 35 U.S.C. §103 as allegedly unpatentable over Bassols et al., J. Biol. Chem., **263**:3039-3045 (1988) in view of Conner et al., supra, and Dasch et al. (U.S. Patent 5,571,714), is respectfully traversed. It is respectfully submitted that this rejection has been rendered moot by the Rule 131 Declaration submitted herewith, establishing that the Conner reference has been antedated and cannot be used as prior art,

Inventors: Border and Ruoslahti
Serial No.: 08/349,479
Filed: December 2, 1994
Page 6

as discussed above. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

In addition, it is respectfully submitted that the Dasch '714 patent has been antedated by the accompanying Rule 131 Declaration, in which conception of the claimed methods is established prior to December 22, 1988, by the inventors explicit averments under oath and Exhibits A-C, and diligent reduction to practice is established by Exhibits D and E; as set forth above. Therefore, similar to the Conner and MacKay references, the Dasch '714 patent has been antedated and cannot be used as prior art in any new rejections.

The provisional rejection of claims 21-23 and 25 under the doctrine of obviousness-type double patenting as allegedly unpatentable over claims 27, 30, 35 and 36 of copending application Serial No. 08/458,864, is respectfully traversed. The claims in the '864 application are directed to:

A method of treating a pathology caused by a TGF- β regulated activity comprising administering to an individual in need thereof, an effective amount of purified **decorin** such that TGF- β is contacted with decorin, whereby the pathology causing activity is prevented or reduced.

Inventors: Border and Ruoslahti
Serial No.: 08/349,479
Filed: December 2, 1994
Page 7

Applicants respectfully disagree with the Examiner's
assertion that:

Although the conflicting claims are not identical, they are not patentably distinct from each other because the two versions of the claims both recite the same method of inhibiting the TGF β -induced promotion of extracellular matrix production which comprises administering an inhibitor of TGF β .

It is respectfully submitted that a method using **decorin** does not suggest any information regarding the use of an **anti-TGF- β** . Thus, a mere disclosure of contacting TGF- β with **decorin** to treat a pathology in no way discloses or suggests the use of **anti-TGF- β** to bind to TGF- β to suppress the deleterious accumulation of TGF- β -induced extracellular matrix in the tissue. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

It is respectfully submitted that because the claims of copending application Serial No. 08/458,864, do not conflict with the instant claims, as set forth above, the requirement under Rule 1.78(c) has been rendered moot.

The provisional rejection of claims 13-15 and 19-21 under the doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-8, 12-18, and 22 of copending application Serial No. 08/457,709, is respectfully traversed. Because claims 13-15, 19 and 20 have been canceled in the instant application (see, e.g., Paper No. 42 dated April 1, 1996, and the like), it is respectfully

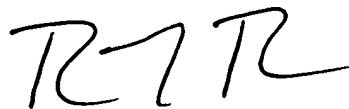
Inventors: Border and Ruoslahti
Serial No.: 08/349,479
Filed: December 2, 1994
Page 8

submitted the this rejection is moot as to those claims. In the '709 application, claims 9-11 are pending, and all other claims have been withdrawn from consideration. However, Applicants will formally cancel the non-elected claims in the '709 application to obviate this rejection. Accordingly, reconsideration and withdrawal of this provisional rejection is respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all pending claims is respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,



Date: August 25, 1999

Robert T. Ramos
Registration No. 37,915
Telephone: (619) 535-9001
Facsimile: (619) 535-8949

CAMPBELL & FLORES LLP
4370 La Jolla Village Drive, Suite 700
San Diego, California 92122

Attachments:

- A - Terminal Disclaimer with Exhibit 1
- B - Rule 131 Declaration of Drs. Ruoslahti and Border with Exhibits A through E